



GRN gene

granulin precursor

Normal Function

The *GRN* gene provides instructions for making a protein called granulin (also known as progranulin). This protein is found in tissues throughout the body. It is most active in cells that are dividing rapidly, such as skin cells and cells that line the gastrointestinal tract. Granulin helps regulate the growth, division, and survival of these cells. It also plays important roles in early embryonic development, regulation of the body's immune system response, and wound healing.

Granulin is active in several types of brain cells, although much less is known about this protein's function in the brain. It appears to be critical for the survival of nerve cells (neurons).

Health Conditions Related to Genetic Changes

GRN-related frontotemporal dementia

More than 65 mutations in the *GRN* gene have been identified in people with *GRN*-related frontotemporal dementia. The most common mutation, which is written as Arg493Ter or R493X, creates a premature stop signal in the instructions for making granulin. Most of the mutations that cause *GRN*-related frontotemporal dementia prevent any protein from being produced from one copy of the *GRN* gene in each cell. As a result of these genetic changes, cells make only half the usual amount of granulin.

It is unclear how a shortage of granulin leads to the features of *GRN*-related frontotemporal dementia. However, studies have shown that the disorder is characterized by the buildup of a protein called TAR DNA-binding protein (TDP-43) in certain brain cells. The TDP-43 protein forms clumps (aggregates) that may interfere with cell functions and ultimately lead to cell death. Researchers are working to determine how mutations in the *GRN* gene, and the resulting loss of granulin, are related to a buildup of TDP-43 in the brain.

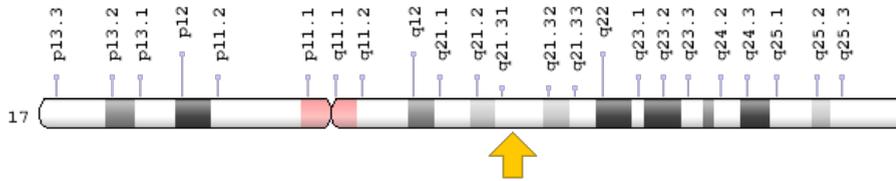
The features of *GRN*-related frontotemporal dementia result from the gradual loss of neurons in regions near the front of the brain called the frontal and temporal lobes. The frontal lobes are involved in reasoning, planning, judgment, and problem-solving, while the temporal lobes help process hearing, speech, memory, and emotion. The death of neurons in these areas causes problems with many critical brain functions. However, it is unclear why the loss of neurons occurs in the frontal and temporal

lobes more often than other brain regions in people with *GRN*-related frontotemporal dementia.

Chromosomal Location

Cytogenetic Location: 17q21.31, which is the long (q) arm of chromosome 17 at position 21.31

Molecular Location: base pairs 44,345,086 to 44,353,106 on chromosome 17 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- acrogranin
- CLN11
- GEP
- GP88
- granulin
- granulin-epithelin
- granulins
- granulins precursor
- GRN_HUMAN
- PC cell-derived growth factor
- PCDGF
- PEPI
- PGRN
- proepithelin
- progranulin

Additional Information & Resources

GeneReviews

- GRN-Related Frontotemporal Dementia
<https://www.ncbi.nlm.nih.gov/books/NBK1371>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GRN%5BTIAB%5D%29+OR+%28granulin%5BTIAB%5D%29+OR+%28PGRN%5BTIAB%5D%29+OR+%28progranulin%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- GRANULIN PRECURSOR
<http://omim.org/entry/138945>

Research Resources

- Alzheimer Disease & Frontotemporal Dementia Mutation Database
<http://www.molgen.ua.ac.be/FTDMutations/Default.cfm?MT=1&ML=0&Page=Contexts&ID=5>
- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/GRNID40757ch17q21.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=GRN%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4601
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/2896>
- UniProt
<http://www.uniprot.org/uniprot/P28799>

Sources for This Summary

- Baker M, Mackenzie IR, Pickering-Brown SM, Gass J, Rademakers R, Lindholm C, Snowden J, Adamson J, Sadovnick AD, Rollinson S, Cannon A, Dwosh E, Neary D, Melquist S, Richardson A, Dickson D, Berger Z, Eriksen J, Robinson T, Zehr C, Dickey CA, Crook R, McGowan E, Mann D, Boeve B, Feldman H, Hutton M. Mutations in progranulin cause tau-negative frontotemporal dementia linked to chromosome 17. *Nature*. 2006 Aug 24;442(7105):916-9. Epub 2006 Jul 16. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16862116>
- Bateman A, Bennett HP. The granulin gene family: from cancer to dementia. *Bioessays*. 2009 Nov; 31(11):1245-54. doi: 10.1002/bies.200900086. Review. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19795409>
- Cruts M, Gijselinck I, van der Zee J, Engelborghs S, Wils H, Pirici D, Rademakers R, Vandenberghe R, Dermaut B, Martin JJ, van Duijn C, Peeters K, Sciot R, Santens P, De Pooter T, Mattheijssens M, Van den Broeck M, Cuijt I, Vennekens K, De Deyn PP, Kumar-Singh S, Van Broeckhoven C. Null mutations in progranulin cause ubiquitin-positive frontotemporal dementia linked to chromosome 17q21. *Nature*. 2006 Aug 24;442(7105):920-4. Epub 2006 Jul 16. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16862115>
- Cruts M, Van Broeckhoven C. Loss of progranulin function in frontotemporal lobar degeneration. *Trends Genet*. 2008 Apr;24(4):186-94. doi: 10.1016/j.tig.2008.01.004. Epub 2008 Mar 6. Review. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18328591>
- Eriksen JL, Mackenzie IR. Progranulin: normal function and role in neurodegeneration. *J Neurochem*. 2008 Jan;104(2):287-97. Epub 2007 Oct 22. Review. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17953663>
- Gass J, Cannon A, Mackenzie IR, Boeve B, Baker M, Adamson J, Crook R, Melquist S, Kuntz K, Petersen R, Josephs K, Pickering-Brown SM, Graff-Radford N, Uitti R, Dickson D, Wszolek Z, Gonzalez J, Beach TG, Bigio E, Johnson N, Weintraub S, Mesulam M, White CL 3rd, Woodruff B, Caselli R, Hsiung GY, Feldman H, Knopman D, Hutton M, Rademakers R. Mutations in progranulin are a major cause of ubiquitin-positive frontotemporal lobar degeneration. *Hum Mol Genet*. 2006 Oct 15;15(20):2988-3001. Epub 2006 Sep 1. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16950801>
- Le Ber I, van der Zee J, Hannequin D, Gijselinck I, Campion D, Puel M, Laquerrière A, De Pooter T, Camuzat A, Van den Broeck M, Dubois B, Sellal F, Lacomblez L, Vercelletto M, Thomas-Antérion C, Michel BF, Golfier V, Didic M, Salachas F, Duyckaerts C, Cruts M, Verpillat P, Van Broeckhoven C, Brice A; French Research Network on FTD/FTD-MND. Progranulin null mutations in both sporadic and familial frontotemporal dementia. *Hum Mutat*. 2007 Sep;28(9):846-55. *Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17436289>

- Rademakers R, Baker M, Gass J, Adamson J, Huey ED, Momeni P, Spina S, Coppola G, Karydas AM, Stewart H, Johnson N, Hsiung GY, Kelley B, Kuntz K, Steinbart E, Wood EM, Yu CE, Josephs K, Sorenson E, Womack KB, Weintraub S, Pickering-Brown SM, Schofield PR, Brooks WS, Van Deerlin VM, Snowden J, Clark CM, Kertesz A, Boylan K, Ghetti B, Neary D, Schellenberg GD, Beach TG, Mesulam M, Mann D, Grafman J, Mackenzie IR, Feldman H, Bird T, Petersen R, Knopman D, Boeve B, Geschwind DH, Miller B, Wszolek Z, Lippa C, Bigio EH, Dickson D, Graff-Radford N, Hutton M. Phenotypic variability associated with progranulin haploinsufficiency in patients with the common 1477C-->T (Arg493X) mutation: an international initiative. *Lancet Neurol.* 2007 Oct;6(10):857-68. Erratum in: *Lancet Neurol.* 2007 Dec;6(12):1037.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17826340>
 - Yu CE, Bird TD, Bekris LM, Montine TJ, Leverenz JB, Steinbart E, Galloway NM, Feldman H, Woltjer R, Miller CA, Wood EM, Grossman M, McCluskey L, Clark CM, Neumann M, Danek A, Galasko DR, Arnold SE, Chen-Plotkin A, Karydas A, Miller BL, Trojanowski JQ, Lee VM, Schellenberg GD, Van Deerlin VM. The spectrum of mutations in progranulin: a collaborative study screening 545 cases of neurodegeneration. *Arch Neurol.* 2010 Feb;67(2):161-70. doi: 10.1001/archneurol.2009.328.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20142524>
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